The Selective Cleavage of Aromatic Benzyl Ethers with Magnesium Bromide via Neighbouring Group Effect

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The use of ethers as stable protecting groups for the hydroxyl group is ubiquitous in organic synthesis.^{1–3} In this regard, benzyl ethers are among the most versatile owing to their ease of formation, inherent stability and the variety of available deprotection methods. Various Lewis acids such as aluminum and boron trihalides have been used as ether-cleaving agents,^{1,2} in particular AlCl_3 ⁴ and BCl_3 ⁵, for selective cleavage of aromatic methoxy groups adjacent to a carbonyl function without affecting other methoxy groups present in the molecule. Such specificity is one of the desirable features of an ether-cleaving agent, but little systematic work appears to have been done in this area. The selective cleavage of the more reactive benzyl ethers would be expected to require less powerful and thus more selective cleaving agents. We have found such a reagent,

namely, anhydrous magnesium bromide in a benzene/ether mixture. Thus, when the aromatic dibenzyloxy aldehydes 1–5 were treated under gentle reflux for 24 h with one equivalent of freshly prepared magnesium bromide⁶ in 7:1 benzene/ether solution, selective debenzylation took place in good to excellent yields (Table 1). The preparation of the aromatic dibenzyloxy aldehydes took place by *bis*-benzylation of the corresponding dihydroxy-benzene and -naphthalene derivatives, followed by Vilsmeier formylation.⁷

We believe that selective deprotection involves the complex 6, Scheme 1, followed by bromide ion displacement to complex 7, isolable as a yellow, moisture-sensitive solid, but not characterized and hydrolysed to the product. That an intermediate of the type 6 was indeed involved is supported by the fact that, immediately after the

Table 1. Reaction of MgBr_2 with aromatic dibenzyloxy aldehydes^a

Dibenzyloxy aldehyde		Product	Yield/%
2,3-Dibenzyloxybenzaldehyde	1	3-Benzyloxy-2-hydroxybenzaldehyde	72
2,4-Dibenzyloxybenzaldehyde	2	4-Benzyloxy-2-hydroxybenzaldehyde	94
2,5-Dibenzyloxybenzaldehyde	3	5-Benzyloxy-2-hydroxybenzaldehyde	95
2,6-Dibenzyloxy-1-naphthaldehyde	4	6-Benzyloxy-2-hydroxy-1-naphthaldehyde	63
2,7-Dibenzyloxy-1-naphthaldehyde	5	7-Benzyloxy-2-hydroxy-1-naphthaldehyde	70

^aAll new compounds were fully characterized spectroscopically and/or by elemental analysis.

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Scheme 1

addition of MgBr_2 to the solution of **5**, a green yellow complex was formed. When this complex was stirred overnight at room temperature, no change occurred and hydrolysis at this stage led to quantitative recovery of starting material. On the other hand, when **6** was gently refluxed, a change in colour occurred, presumably as a result of formation of **7**, the hydrolysis of which gave the desired product.

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